PTO/SB/08 (09-06)

Approved for use through 03/31/2007. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid

Control number.

| Substitute for form 1449/PTO |
|------------------------------|
| INFORMATION DISCLOSURE |
| STATEMENT BY APPLICANT |

Date Submitted: April 1, 2009

(use as many sheets as necessary)

Sheet 1 of 3

| Complete if Known | | | | |
|------------------------|-------------------|--|--|--|
| Application Number | 10/677,227 | | | |
| Filing Date | 10/3/2003 | | | |
| First Named Inventor | Hiroaki ITO | | | |
| Art Unit | 1646 | | | |
| Examiner Name | Prema Maria MERTZ | | | |
| Attorney Docket Number | 053466-0365 | | | |

| U.S. PATENT DOCUMENTS | | | | | | | |
|-----------------------|------|--|------------------|----------------------------------|--|--|--|
| Examin er Cite No.1 | Cite | Document Number | Publication Date | Name of Patentee or Applicant of | Pages, Columns, Lines, Where Relevant | | |
| | | Number-Kind Code ² (if known) | MM-DD-YYYY | Cited Document | Passages or Relevant Figures Appear | | |
| | E1 | 2002/0187150 A1 | 12/12/2002 | Mihara et al. | | | |
| | E2 | 2003/0236260 A1 | 12/25/2003 | Shimojo et al. | | | |
| | E3 | 2004/0115197 A1 | 06/17/2004 | Yoshizaki et al. | | | |
| | E4 | 2006/0292147 A1 | 12/28/2006 | Yoshizaki et al. | | | |
| | E5 | 5,210,075 A | 05/11/1993 | Scholz et al. | | | |
| | E6 | 5,670,373 A | 09/23/1997 | Kishimoto, Tadamitsu | | | |
| | | | | | | | |
| | | | | | | | |

| | | | FOREIGN PATENT | DOCUMENTS | | |
|-----------------------|--------------------------|--|--------------------------------|---|--|----|
| Examiner Initials* | Cite No. ¹ | Foreign Patent Document Country Code ³ Number ⁴ Kind Code ⁵ (<i>if known</i>) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Documents | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T€ |
| | E7 | EP 0 448 181 A2 | 09/25/1991 | Gist-Brocades N.V. | | |
| | E8 | EP 0 628 639 A1 | 12/14/1994 | Chugai Seiyaku Kabushiki Kaisha | | |
| | E9 | EP 0 785 276 A1 | 07/23/1997 | Ajinomoto Co., Inc. | | |
| | E10 | EP 0 791 359 A1 | 08/27/1997 | Chugai Seiyaku Kabushiki Kaisha | | |
| | E11 | WO 95/09873 A1 | 04/13/1995 | Board of Regents, The University of Texas System | | |
| | E12 | WO 95/13086 A1 | 05/18/1995 | Houghten Pharmaceuticals, Inc. | | |
| - | E13 | WO 95/34320 A2 | 12/21/1995 | Regents of the University of Minnesota | | |
| | E14 | WO 96/33735 A1 | 10/31/1996 | Cell Genesys, Inc. | | |
| | E15 | WO 98/25971 A1 | 06/18/1998 | Celltech Therapeutics Limited | | |
| | E16 | WO 98/28001 A1 | 07/02/1998 | Advanced Biotherapy Concepts, Inc. | | |
| | E17 | WO 2004/096273 A1 | 11/11/2004 | Chugai Seiyaku Kabushiki Kaisha | | |

| NON PATENT LITERATURE DOCUMENTS | | | | | | |
|---------------------------------|--------------|--|----|--|--|--|
| Examiner Initials* | Cite No.1 | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | Te | | | |

| Examiner Signature | /Prema Mertz/ | Date Considered | 06/02/2010 |
|-----------------------|---------------|--------------------|------------|

"EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| | Substitute for fo | orm 14 | 49/PTO | Complete if Known | | |
|-------|-----------------------------------|----------|---------|------------------------|-------------------|--|
| | INFORMATION | DISC | LOSURE | Application Number | 10/677,227 | |
| | STATEMENT B | YAPE | PLICANT | Filing Date | 10/3/2003 | |
| | Date Submitted: April 1, 2009 | | | First Named Inventor | Hiroaki ITO | |
| | Date Submitted | ı. Apııı | 1, 2009 | Art Unit | 1646 | |
| | (use as many sheets as necessary) | | | Examiner Name | Prema Maria MERTZ | |
| Sheet | 2 | of | 3 | Attorney Docket Number | 053466-0365 | |

| | | NON PATENT LITERATURE DOCUMENTS | |
|-----------------------|--------------------------|--|----------------|
| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ⁶ |
| | E18 | -Office-Action-in-counterpart-Shileon-Application-1241-2004,-7-pages- | |
| | E19 | ATREYA et al., "Blockade of interleukin 6 trans signaling suppresses T-cell resistance against apoptosis in chronic intestinal inflammation: Evidence in Crohn disease and experimental colitis in vivo," Nature Medicine, May 2000, 6(5):583-588. | |
| | E20 | GAILLARD et al., "Identification of a novel antigenic structure of the human receptor for interleukin-6 involved in the interaction with the glycoprotein 130 chain," Immunology, 1996, 89:135-141. | |
| | E21 | GROTTRUP-WOLFERS et al., "Elevated cell-associated levels of interleukin 1 β and interleukin 6 in inflamed mucosa of inflammatory bowel disease," European Journal of Clinical Investigation, 1996, 26:115-122. | |
| | E22 | HOLUB et al., "Increased Interleukin-6 Levels, Interkeukin-6 Receptor and gp130 Expression in Peripheral Lymphocytes of Patients with Inflammatory Bowel Disease," Scand. J. Gastorenterol., 1998, 33 Suppl., 223:47-50. | |
| | E23 | ITO et al., "A Pilot Randomized Trial of a Human Anti-Interleukin-6 Receptor Monoclonal Antibody in Active Crohn's Disease," Gastroenterology, 2004, 126(4):989-996. | |
| | E24 | ITO et al., "Anti-IL-6 receptor monoclonal antibody inhibits leukocyte recruitment and promotes T-cell apoptosis in a murine model of Crohn's disease," J. Gastroenterol., 2002, 37(Supp. 14):56-51. | |
| | E25 | ITO et al., "IL-6 and Crohn's Disease," Current Drug Targets - Inflammation & Allergy, 2003, 2(2):125-130. | |
| | E26 | JONES et al., "Mucosal Interleukin-6 Secretion in Ulcerative Colitis," Scand. J. Gastroenterol., 1994, 29:722-728. | |
| | E27 | KALAI et al., "Analysis of the mechanism of action of anti-human interleukin-6 and anti-human interleukin-6 receptor-neutralising monoclonal antibodies," Eur. J. Biochem., 1997, 249:690-700. | |
| | E28 | KIBERD, Bryce A., "Interleukin-6 Receptor Blockage Ameliorates Murine Lupus Nephritis," Journal of the American Society of Nephrology, 1993, 4(1):58-61. | |
| | E29 | KISHIMOTO, Tadamitsu, "Interleukin-6 and its Receptor in Autoimmunity," Journal of Autoimminuty, 1992, 5(Supp. A):123-132. | |
| | E30 | KITANI et al., "Autostimulatory effects of IL-6 on excessive B cell differentiation in patients with systemic lupus erythematosus: analysis of IL-6 production and IL-6R expression," Clin. Exp. Immunol, 1992, 88:75-83. | |

| | | | |
|-----------------------|---------------|--------------------|------------|
| Examiner Signature | /Prema Mertz/ | Date Considered | 06/02/2010 |

*EXAMINER: Initial if reference considered; whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| | Substitute for fo | orm 1449/F | ото | C | omplete if Known |
|------------------------|-------------------------------|------------|----------|------------------------|-------------------|
| | INFORMATION | DISCLOS | SURE | Application Number | 10/677,227 |
| STATEMENT BY APPLICANT | | | CANT | Filing Date | 10/3/2003 |
| | Date Submitted: April 1, 2009 | | | First Named Inventor | Hiroaki ITO |
| | Date Submitted | Aprii 1, | 2009 | Art Unit | 1646 |
| | (use as many shee | ets as nec | cessary) | Examiner Name | Prema Maria MERTZ |
| Sheet | 3 | of 3 | | Attorney Docket Number | 053466-0365 |

| | | NON PATENT LITERATURE DOCUMENTS | | | |
|-----------------------|--|--|--|--|--|
| Examiner Initials* | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published. | | | | |
| | E31 | KUSUGAMI et al., "Elevation of Interleukin-6 in Inflammatory Bowel Disease is Macrophage- and Epithelial Cell-Dependent," Digestive Diseases and Sciences, May 1995, 40(5):949-959. | | | |
| | E32 | NAGAFUCHI et al., "Constitutive Expression of IL-6 Receptors and Their Role in the Excessive B Cell Function in Patients with Systemic Lupus Erythematosus," J. Immunol., December 1, 1993, 151(11):6525-6534. | | | |
| | E33 | STEVENS et al., "Tumor Necrosis Factor-α, Interleukin-1β, and Interleukin-6 Expression in Inflammatory Bowel Disease," Digestive Diseases and Sciences, June 1992, 37(6):818-826. | | | |
| | E34 | SUZUKI et al., "Anti-murine IL-6 receptor antibody inhibits IL-6 effects in vivo," Immunology Letters, 1991, 30:17-22. | | | |
| * | E35 | VANDENABEELE et al., "Increased IL-6 Production and IL-6-Mediated Ig Secretion in Murine Host-vs-Graft Disease," J. Immunol., May 1, 1993, 150(9):4179-4187. | | | |

| Examiner Signature | /Prema Mertz/ | Date Considered | 06/02/2010 |
|-----------------------|---------------|--------------------|------------|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.